

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claims 100 – 109, 111, 114 – 121, 123, 127, 129, 131 – 137, 140, 143, 144 (canceled).

144. (presently amended): A method of regulating ~~a transient~~ expression of a desired protein or RNA in ~~an~~ a non-human animal *in vivo*, the method comprising:

administering to the animal a pharmacological dose of a ligand, wherein the ligand is an antagonist for a non-mutated steroid hormone receptor protein,

wherein the animal comprises:

(a) ~~a first nucleic acid cassette comprising a coding sequence of encoding~~ a molecular switch comprising a mutated receptor protein, wherein the mutated receptor protein comprises:

~~a non-steroid hormone receptor~~ DNA binding domain which binds a promoter that is transcriptionally linked to a target gene;

~~a mutated steroid hormone receptor superfamily ligand binding domain which is distinct from a naturally occurring ligand binding domain, has an alternation in C terminal amino acids and binds the ligand by one or more alternations that reverse a ligand specificity of the receptor and confer activation by the antagonist;~~

a transactivation domain which causes a transcription from the promoter when the molecular switch is bound to the promoter and the ligand; and

(b) ~~a second nucleic acid cassette comprising the~~ target gene transcriptionally linked to the promoter,

wherein administration of the ligand regulates expression ~~of the desired protein or RNA in the animal from the target gene.~~

145. (previously added): The method of claim 144, wherein the mutated steroid hormone superfamily receptor ligand binding domain is selected from the group consisting of estrogen, progesterone, androgen, Vitamin D, COUP-TF, cis-retinoic acid, Nurr-1, thyroid hormone, mineralocorticoid, glucocorticoid-alpha, glucocorticoid-beta, and orphan receptor ligand binding domains.

146. (currently amended): The method of claim 144 wherein the mutated receptor protein is a mutated progesterone receptor ~~and the DNA binding domain is a non steroid hormone DNA binding domain.~~

147. (currently amended): The method of claim 144, wherein the ~~first nucleic acid cassette and the second nucleic acid cassette in the animal are on separate plasmids target gene and promoter are encoded on a nucleic acid cassette that has been introduced into the animal.~~

148. (currently amended): The method of claim 144, wherein the non-steroid hormone receptor DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or, a modified DNA binding domain.

149. (currently amended): The method of claim 144, wherein the animal is a transgenic mammal.

150. (currently amended): The method of claim ~~149~~ 144, wherein the mammal is a human transgenic nucleic acid encoding the molecular switch has been introduced into the animal on an expression vector that encodes the molecular switch.

151. (previously added): The method of claim 144, wherein the DNA binding domain is a Gal-4 DNA binding domain.

152. (currently amended): The method of claim 144, wherein the mutated steroid hormone receptor ligand binding domain binds a compound selected from the group consisting of 5 α -pregnane-3, 20-dione; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -propinyl-4, 9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 α -hydroxy-17 β -(3-hydroxypropyl)-13 α -methyl-4,9-gonadiene-3-one; 11 β -(4-acetylphenyl)-17 β -hydroxy-17 α -(1-propinyl)-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17[[α]] α -(3-hydroxy-1 (Z)-propenyl-estra-4, 9-diene-3-one; (7 β ,11 β ,17 β)-11-(4-dimethylaminophenyl)-7-methyl-4', 5'-dihydrospiro(ester-4, 9-diene-17, 2' (3'H)-furan)-3-one; (11 β ,14 β ,17 α)-4',5'-dihydro-11-(4-dimethylaminophenyl)-(spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.

153. (previously added): The method of claim 144, wherein the mutated steroid hormone superfamily receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.

154. (previously added): The method of claim 144, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

155. (previously added): The method of claim 144, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.

156. (previously added): The method of claim 155, wherein the transactivation domain comprises a TAF-1 transactivation domain.

157. (previously added): The method of claim 155, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.

158. (previously added): The method of claim 155, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.

159. (previously added): The method of claim 144, wherein the molecular switch is tissue specific.

160. (previously added): The method of claim 159, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

161. (currently amended): The method of claim ~~159~~ 147, wherein the ~~second nucleic acid cassette comprising the target gene and promoter are encoded in a nucleic acid cassette that further comprises a tissue-specific cis-element.~~

162. (currently amended): The method of claim ~~144~~ 146, wherein the alteration is ~~a deletion of in from about 1 to about 54 naturally occurring carboxyl terminal amino acids in the mutated steroid hormone receptor superfamily progesterone receptor ligand binding domain.~~

163. (previously added): The method of claim 144, wherein the ligand is RU38486.

164. (previously added): The method of claim 144, wherein the ligand is 11 beta-(4-dimethylaminophenyl)-17 beta-hydroxy-17 alpha-propinyl-4,9-estradiene-3-one.

165. (currently amended): The method of claim 144 146, wherein the ligand is an antiprogestrone.

166. (previously added): The method of claim 144, wherein the ligand requires conversion to an active form in an end organ.

167. (previously added): The method of claim 144, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.

168. (currently amended): A method of regulating ~~an transient expression of a desired protein or RNA target gene in an animal~~ *in vivo* comprising:

administering to the animal a pharmacological dose of a ligand that activates a molecular switch encoded by a ~~molecule~~ molecular switch expression cassette, the cassette having been previously administered to the animal for transient expression or is comprised in a non-human transgenic animal comprised in the animal, wherein the molecular switch comprises a sequence specific non-steroid hormone receptor DNA binding domain and mutated steroid hormone superfamily receptor ligand binding domain which is characterized by alteration of from about 1 to about 120 naturally occurring C-terminal amino acids of the ligand binding domain of a corresponding wild type steroid hormone superfamily receptor and is activated by the ligand which is not a native ligand for the corresponding wild type steroid hormone superfamily receptor ~~ligand binding domain~~ and wherein the activation of the molecular switch results in binding to a specific DNA sequence in the regulatory region of a target gene promoter and ~~results in the expression of the desired protein or RNA~~ from the target gene.

169. (previously added): The method of claim 168, wherein the mutated steroid hormone superfamily receptor ligand binding domain is the ligand binding domain of a steroid hormone superfamily receptor selected from the group consisting of: estrogen; progesterone; glucocorticoid- α ; glucocorticoid- β ; mineralcorticoid; androgen; thyroid hormone; retinoic acid; retinoid X; Vitamin D; COUP-TF; ecdysone; Nurr-1 and orphan receptors.

170. (previously added): The method of claim 168, wherein the mutated steroid hormone superfamily receptor ligand binding domain is a mutated progesterone ligand binding domain and the ligand is an anti-progestin.
171. (previously added): The method of claim 170, wherein the anti-progestin is selected from the group consisting of: RU 38486; Org31806; and Org 31376.
172. (previously added): The method of claim 168, wherein DNA binding domain is a non-steroid hormone DNA binding domain.
173. (currently amended): The method of claim 168, wherein the DNA binding domain is selected from the group consisting of: a GAL-4 DNA binding domain; a viral DNA binding domain[[s]]; an insect DNA binding domain[[s]]; and a non-mammalian DNA binding domains.
174. (previously added): The method of claim 168, wherein the molecular switch further comprises a transactivation domain distinct from a steroid hormone receptor superfamily transactivation domain.
175. (previously added): The method of claim 168, wherein the transient expression is up-regulated.
176. (currently amended): The method of claim ~~135~~ 168, wherein the transient expression is down-regulated.

177. (currently amended): A method of regulating a transient expression of a desired protein or RNA in an animal *in vivo*, the method comprising:

administering to the animal a pharmacological dose of a ligand, wherein the ligand is an antagonist for a non-mutated progesterone receptor protein,

wherein the animal ~~comprises~~ has been previously administered a coding sequence of a molecular switch comprising a mutated progesterone receptor protein, wherein the mutated progesterone receptor protein comprises:

a DNA binding domain specific for a DNA site on a promoter transcriptionally linked to a target gene;

a mutated progesterone receptor ligand binding domain which has ~~a deletion~~ alterations of from 1 to 54 naturally occurring C-terminal amino acids and ~~binds to~~ is activated by the ligand;

a transactivation domain which causes a transcription from the promoter when the molecular switch is bound to the promoter and the ligand; and

wherein administration of the ligand regulates expression of the desired protein or RNA from the target gene.

178. (previously added): The method of claim 177, wherein the DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or a modified DNA binding domain.

179. (previously added): The method of claim 177, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

180. (previously added): The method of claim 177, wherein the animal is a mammal.

181. (previously added): The method of claim 180, wherein the mammal is a human.

182. (currently amended): The method of claim 177, wherein the ligand selected from the group consisting of 5 α -pregnane-3,20-dione; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -propinyl-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 α -hydroxy-17 β -(3-hydroxypropyl)-13 α -methyl-4,9-gonadiene-3-one; 11 β -(4-acetylphenyl)-17 β -hydroxy-17 α [[-]]-[1-propinyl]-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17[[-]] α -[[-]](3-hydroxy-1 (Z)-propenyl)-estra-4,9-diene-3-one; (7 β ,11 β ,17 β)-11-(4-dimethylaminophenyl)-7-methyl-4',5'-dihydrospiro(ester-4,9-diene-17,2'(3'H)-furan)-3-one; (11 β ,14 β ,17 α)-4',5'-dihydro-11-(4-dimethylaminophenyl)- (spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.
183. (previously added): The method of claim 177 wherein the ligand is an anti-progesterone.
184. (previously added): The method of claim 183 wherein the antiprogestrone is RU 34846, Org 3186, or Org 31376.
185. (previously added): The method of claim 177, wherein the mutated progesterone receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.
186. (previously added): The method of claim 177, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.
187. (previously added): The method of claim 177, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.
188. (previously added): The method of claim 177, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.
189. (previously added): The method of claim 177, wherein the molecular switch is tissue specific.
190. (previously added): The method of claim 189, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

191. (previously added): The method of claim 190, wherein the target gene further comprises a tissue-specific cis-element.

192. (previously added): The method of claim 177, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.